EXHIBIT 1
to
REQUEST FOR RECONSIDERATION DATED APRIL 7, 2010

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Patel, et al. Serial No. 10/613,698 Filed: July 3, 2003 Attorney Docket No.: 03-40102-US	DELIVERY SYSTEM FOR TOPICAL MEDICATIONS

DECLARATION OF EUGENE H. GANS, Ph.D.

I, Eugene H. Gans, Ph.D., hereby declare that:

A. Introduction

1. I am one of the inventors in this Application, U.S. Patent Application No. 10/613,698.

2. I received a Bachelor of Science (B.S.) in 1951 from Colombia University, New York, New York; a Master of Science (M.S.) in 1953 from Columbia University, New York, New York; a Doctor of Philosophy (Ph.D.) in 1956 from the University of Wisconsin, Madison, Wisconsin.

3. I am inventor of numerous patents in the field of dermatologic products and dermatologic formulations and have worked in this field for over 40 years.

4. I am very familiar with the knowledge and skills possessed by persons skilled in this field.

5. I have read the Office Action dated October 27, 2009 in this Application. In particular, I have read the portion of the Office Action where some of the claims are rejected because the Examiner believes that the application does not enable one to practice the invention.

6. The specification of this Application enables one of ordinary skill in the art to practice the claimed invention. Among other things, the specification enables one skilled in the art to make and use (1) the compositions described in the claims having any insoluble dermatologically active ingredient, and (2) the compositions having active ingredients in the full range of particle sizes described in the claims.

B. Disclosures Concerning Insoluble Dermatologically Active Ingredients

7. Persons skilled in the art of dermatologic formulations are highly familiar with insoluble, dermatologically active ingredients. These ingredients have been widely used for decades (in some cases, almost a century). The selection, preparation and use of these ingredients is part of the essential repertoire of any person skilled in the art of dermatologic formulations.

8. Several examples of insoluble dermatologically active ingredients are given in the specification of this application. (See. e.g. ¶16). More such ingredients are described in standard dermatologic references. See, e.g. *Harry's Cosmeticology*, 6th Ed. pp. 107-108, 116-117, 249, 331 attached as Exhibit A to Declaration of Eugene H. Gans, Ph.D. Still others are well known to persons skilled in the art of dermatologic formulations.

9. At paragraph 16, the application describes zinc oxide, iron EDTA, magnesium peroxide, minocycline, hydrocortisone, BPO and sulfur as examples of insoluble dermatologically active ingredients.

10. In *Harry's Cosmeticology*, colloidal kaolin (pp. 107-108; 116-117), zinc oxide (pp. 107; 331), talcum powder (p. 249), colloidal calamine (p. 331), are disclosed as insoluble dermatologically active ingredients.

11. The long-standing use of these insoluble, dermatologically active ingredients can be specifically illustrated as follows. BPO has been used since 1958. The medicinal uses of sulfur and sulfur compounds date back at least as early as the days of Pliny the Elder.

12. The physical and chemical properties of insoluble dermatologically active ingredients are well known to one skilled in this art. Their stability, their reactivity with other ingredients, their biochemical effects, and a host of other properties are well known or readily available to persons skilled in this art. Thus, it is well within the knowledge and skill of one skilled in this art to make dermatologic formulations with insoluble dermatologic ingredients.

13. This base of well-established and widely shared knowledge, taken together with the disclosures found in the application, would make it a routine matter for one skilled in the dermatologic art to practice the claimed invention using any insoluble dermatologically active ingredient.

C. Disclosures Concerning Particle Size

14. Persons skilled in the art of dermatologic formulations are highly familiar with using particles of various sizes in topical formulations. Persons skilled in this art have long-standing familiarity with controlling this physical parameter when making topical dermatologic products.

15. The techniques for obtaining and controlling particle size in this context have been known for decades to persons skilled in this art. These techniques include milling and grinding, as well as a variety of sieving and washing techniques. The broad array of techniques that are within the repertoire of dermatologic formulations enables them to produce insoluble dermatologically active ingredients having almost any particle size that might be desired. Persons skilled in the art would simply select whichever of the well-known techniques for obtaining particle size was best suited to result in obtaining the desired size for the particular insoluble dermatologically active ingredient.

16. The milling and grinding technologies that are well known to one skilled in this field include the use of devices such as direct drive mills, ball mills, roller mills, cyclone mills, hammer mills, jar mills, Glatt mills, Raymond mills, Fitzpatrick mills, and Patterson-Kelley machines. Even a mortar and pestle, long a symbol of the profession of pharmacy, can be used to produce particles of the desired size.

17. The claims of the application specify certain particle size. Claim 34 calls for the particles to be up to about 300 microns. Claim 35 calls for the particles to be less than about 50 microns. Claim 5 calls for the particles to be in the range of from about 10 to about 150 microns. All of these particle sizes are easily obtained using the above mentioned techniques.

18. These well-known techniques, together with the disclosures contained in the application, would enable a person skilled in this art to make and use the compositions described in the claims.

19. Persons working in this field have long been familiar with insoluble particle dermatology active ingredients, and with techniques for controlling the size of these particles. However, the inventors and I were the first to discover that the regulation of particle size and viscosity, as called for in the claims of this application, would enable an emulsion containing these ingredients to be reliably applied to a pad or cloth, and yet obtain excellent release of the insoluble particulate active ingredient to the skin.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any registration resulting therefrom.

Date: 3/19/10

Eugene H. Gans, Ph.D.

EXHIBIT A
to
DECLARATION OF EUGENE H. GANS, PH.D.

Harry's Cosmeticology

being the sixth edition of
THE PRINCIPLES AND PRACTICE OF MODERN COSMETICS
VOLUME ONE by

RALPH G. HARRY, F.R.I.C., F.R.S.M., A.S.P.S.

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CHEMICAL PUBLISHING CO., INC.
New York 1973

First published by
Leonard Hill Books
a division of
International Textbook Company Limited
Kingswood House, Heath & Reach, Leighton Buzzard, Beds. LU7 0AZ

First edition (New York)	1940
Second edition (London)	1944
Reprinted	1946
Reprinted	1952
Third edition (New York)	1947
Fourth edition (London)	1955
Fifth edition (London)	1962
Sixth edition (London)	1973

Published in the USA by Chemical Publishing Co. Inc.,
200 Park Avenue South, New York, N.Y. 1003

Patents

In this book, the patent literature has been treated as a source of information.

Certain formulae and processes have been included in the interests of science, notwithstanding the existence of actual or potential patent rights.

Mention of a patent does not necessarily indicate that the patent is currently in force, but in so far as materials and processes are protected by Letters Patent, their inclusion neither conveys nor implies licence to manufacture.

Each manufacturer should ascertain for himself the patent position existing in his own country at that time.

Legislation

Legislation concerned with permitted materials, limitations on use and methods of sale of toilet preparations is in a state of continual change, notably in U.S.A. and the European Economic Community. Whilst every effort has been made to take count of the latest position, inclusion of a particular ingredient in any one illustrative formula cannot be taken as indicating that this formula will be within the limits of legal permission in any one country at the time when it may be under consideration. As with Patents (above) every manufacturer must ascertain for himself the legal position existing in his country or that to which he exports at that time.

Printed in Great Britain

Finally, the use of polyvinyl pyrrolidone in face packs is illustrated by a model formula quoted from a technical bulletin (3):

	per cent.
PVP K–15	3·0
Methyl cellulose (low viscosity)	9·0
Glycerine	7·5
Water	80·5
Insoluble opacifiers, perfume, preservative	*q.s.*

EARTH-BASED SYSTEMS (ARGILLACEOUS MASKS)

Products in this group are often referred to as paste masks. They include clay facial packs and the so-called mud packs and usually contain a high percentage of solids.

These products can either be presented in bulk, or packed in sachets, for mixing with water when required, or they can be presented ready mixed for use. In the latter case it is advisable to pre-sterilize by heating and to incorporate a suitable preservative as many of the natural earths are heavily contaminated with micro-organisms.

As the mask dries on the face it hardens and contracts again giving the sensation of mechanical astringency. The presence of absorbent clays such as bentonite produces a genuine cleaning effect, particularly on very greasy skins.

China clay, colloidal kaolin, fuller's earth, bentonite, etc., may be used as the 'argillaceous' material, the choice depending in part on the criteria which it is proposed to apply to the finished product.

If the colour of fuller's earth or bentonite is considered objectionable, this difficulty may be met by blending with kaolin, and/or the addition of zinc oxide or titanium dioxide.

Bentonite is a colloidal clay derived from volcanic ash found in certain parts of the United States, which is characterized by its strong affinity for water and its thixotropic properties. Certain bentonites will absorb up to fifteen times their volume of water, this property being greatly increased by the addition of a small quantity of magnesium oxide, or some other substance possessing a similar pH.

The wide variations in the analysis of bentonites reported in the literature (4) stem from the considerable variations in different beds in the Benton formation and even in different strata in the same beds.

The consistency of bentonite gels will vary with concentration and will be considerably influenced by the pH of the gels. According to Griffon (5), a gel containing 6% bentonite has the consistency of glycerine, whilst 20% gel has the consistency of lanolin.

Bentonite gels have been described as soothing to the skin (6), and have been claimed to be of value in the treatment of eczema, abscesses, sores and

wounds (7). They have been used in a number of dermatological preparations (8, 9, 10).

The nature of kaolin and its purification to a quality suitable for cosmetic purposes are described in Chapter 12. This type of electrolytically purified kaolin is equally suitable for use in face packs because of its qualities of fineness, softness, moisture adsorption and easy spreading.

Hydrocolloids such as the carragheen gums may be added to stabilize the suspension of solids while contributing to the mechanical strength of the dried film. Again, plasticizers such as glycerine may be added. Special attributes may be conferred by adding additional ingredients such as sulphur (see Chapter 34), astringents, bleaching agents, acids, etc.

The following formulae illustrate this type of product:

All-purpose mask

	per cent.
Kaolin	35·0
Bentonite	5·0
Cetyl alcohol	2·0
Sodium lauryl sulphate	0·1
Glycerine	10·0
Nipagin M	0·1
Perfume	*q.s.*
Water	to 100·0

Winter (2) gives the following two formulations for face packs for dry and greasy skins respectively:

Face Pack for Dry Skin

	parts
Kaolin	80·0
Starch	10·0
Cold cream	20·0
Cetyl alcohol	2·0
Hydrophilic oil	5·0
Water, boric water or infusions	*q.s.*

Procedure

Melt the cold cream and the cetyl alcohol in warm water. Next add the oil, the powders and then the water or other aqueous matter.

Face Pack for Greasy Skin

	parts
Kaolin	80·0
Magnesium carbonate	15·0
Starch	5·0
Tragacanth gum (powdered)	1·0
Water	*q.s.*

These facts should be adequately considered by consumer trials, properly carried out and statistically evaluated. Such consumer trials must be carried out scientifically, as ill-conceived trials can be made to prove anything and often prove nothing.

ABSORBENCY

The second important function of face powders is to eliminate shiny skin in certain facial areas by absorbing sebaceous secretions and perspiration. The prime requirement of a material for this purpose is a high absorptive capacity. The components of face powders which confer this property are colloidal kaolin, starch, precipitated chalk and magnesium carbonate.

The water absorbent properties of face powders or face powder constituents may be determined by the method of Hewitt (3), in which a known weight of the powder is shaken with excess water and filtered under a standard pressure through a Büchner funnel until no more water emerges. The wet powder is then transferred to a weighed, stoppered weighing bottle, and the increase in weight determined. Methods involving the addition of water from a burette, until the powder becomes semi-fluid, are open to the objection that different observers do not obtain concordant results and the end point is not easily determined.

Water absorption is by no means the main characteristic required in a powder; it must also be absorbent for grease. If a person's face is inclined to dryness a more greasy foundation is usually employed. A powder which is not *grease* absorbent will show a shiny nose or face which will necessitate re-powdering. Constituents of higher opacity such as zinc and titanium oxides tend to mask greasiness, while starch, chalks and kaolin absorb only a certain amount of grease.

Colloidal Kaolin

Kaolin, a hydrated aluminium silicate, is a naturally occurring compound. According to Halpern *et al.* (4), kaolin is not a primary mineral but is a generic term applied to several hydrated aluminium silicates. Not all aluminium silicates, however, may be called kaolin. On the basis of X-ray and physical studies Ross and Kerr (5), established that three different groups of clay are classified as kaolin. These clays (kaolinite, nacrite and dickite) have essentially the same formula ($Al_2O_3 \cdot 2SiO_2 \cdot 2H_2O$). Purified grades of kaolin which are light in colour and free from grit and water-soluble impurities should be used for face powders; the most suitable is electrolytically purified kaolin. Ordinary china clay is obtained by elutriation and on microscopic examination mica, quartz and felspar are readily discernible. Pharmaceutical grades of kaolin are obtained by a peptizing process in which the clay is suspended in water containing a suitable electrolyte (e.g. sodium

pyrophosphate) which confers an electrical charge upon the clay and keeps the finer particles in suspension. Removal of the suspension of fine particles, followed by removal of the electric charge (by addition of another electrolyte or by means of an electric field), yields the finest forms of kaolin. One such grade is known as Osmokaolin.

Colloidal kaolin is used in face powders primarily because its high moisture absorption capacity enables it to absorb perspiration. It has also good covering power, excellent grease-resisting properties and it imparts greater skin adhesion properties to the finished product than does talc. Its relatively high density makes it a useful material for controlling the bulking properties of the powders in which it is used. It also helps to reduce the shine of talc which is present. However, it lacks slip, and is inclined to be somewhat harsh. Its proportion in face powders should therefore not exceed 30%.

Starch and Modified Starches

At one time rice starch was used almost exclusively as the base of face powder formulae on account of its excellent absorptive properties, good covering power and the smoothness it imparted to the skin. The latter property was closely related to its small particle size, the average diameter of rice starch granules being 3–8 microns. Objections were, however, raised to the use of starch because of its tendency to cake when exposed to a humid atmosphere or in the presence of excessive skin secretions. McDonough (6) asserted that it readily forms a sticky paste when wet, clogging the pores, and that it is an ideal nutrient, when moist, for bacteria. In addition it coats the hair shaft and so accentuates the downy hair, otherwise unnoticeable, on a woman's face. It was also claimed that because of the tendency of starch to favour bacterial growth, it could give rise to skin irritation when in contact with the skin for any length of time. These assertions led eventually to the replacement of rice starch by talc as the powder base in face powders. However, it must be said that when any degree of bloom is required, there are few materials which can surpass starch.

Decomposition can be reduced in many cases by the addition of perfume; mention of clogged pores refers not to pores but to the openings of the hair follicles. (Pore openings are invisible by ordinary inspection.) There is no proof that starch can cause clogging of such openings.

Special grades of treated starch which will not swell up or agglutinate in the presence of moisture have been developed for the cosmetic industry. For example, ANM starch powders (Neckar-Chemie, GmbH) are starch ethers which are produced by reacting the hydroxyl groups of the starch molecule with tetramethylolacetylenediurea. These materials are claimed to have a good slip, good adhesive properties and covering power, and a

Kaufman (8). An example, illustrating such compositions in emulsion form, in which a modified coconut triglyceride was used to provide a balance between these opposing characteristics, is given below:

	per cent.
Oil Phase	
Lauric/myristic diethanolamide 2:1	10
Lauric diethanolamide 1:1	5
Polyoxyethylene (16) lanolin alcohols	5
Modified coconut triglyceride	5
Perfume	5
Aqueous Phase	
Triethanolamine lauryl sulphate (40·6% soln)	40
Lactic acid	1
Water	29

The two phases were heated separately to 72°C and the oil phase was then added slowly, with agitation, to the aqueous phase. The resulting emulsion was then cooled with stirring and the perfume added at about 48°C.

BODY OR DUSTING POWDERS

In dealing with bath preparations, mention must also be made of body or dusting powders, sometimes referred to as Body Talcs. The components of such powders are similar to those which are used in face powders, except that the aim here is to provide good slip, a cooling effect and good absorbency. Since they are primarily intended for women, emphasis should also be placed on selecting the right perfume at the right level to cover any earthy note of the components.

Absorbency by the powder would be provided by the inclusion of kaolin, magnesium carbonate, precipitated chalk and starch. Slip will be conferred by talc, zinc stearate and magnesium stearate; talc is the main component of such powders at a level of between 60 and 90%, especially if the powder is to be sold as talc, talcum or talcum powder. Well before the Trade Descriptions Act of 1968, it had been held, in a case where chalk had been sold as talcum, that talcum could not be used as a trade name for dusting powder (9). However, in another case (10) in which the 'talcum powder' contained 51·1% talc the case was dismissed. It would seem that, while the term 'talcum' is not synonymous with all types of dusting powder, neither need it refer to 100% talc, and that a powder containing a very substantial proportion of talc can legitimately be described in this way.

Adhesion of the powder will be improved by the presence of kaolin as well as by the zinc or magnesium stearate. Perfume absorption by such powders will be enhanced by the inclusion of either light magnesium carbonate or heavy calcium carbonate.

Calamine lotion type	*per cent.*
Colloidal calamine	20·0
Glycerine	5·0
Water	75·0
Antiseptic	*q.s.*

Nadkarni and Zopf (43) have suggested the following improved calamine lotion:

Zinc oxide	8·0 g
Prepared calamine	8·0 g
Polyethylene glycol 400	8·0 cm³
Polyethylene glycol 400 monostearate	3·0 g
Lime water	60·0 cm³
Water	to 100 cm³

Triethanolamine stearate milks are also soothing:

	per cent.
Triethanolamine stearate	4·80
Liquid paraffin	10·00
Water	85·20
Antiseptic	*q.s.*

If desired 10% colloidal calamine may be added to this mixture, which is prepared by heating the stearate and oil to 70°C and adding to the water at the same temperature, or preferably by preparing the triethanolamine stearate *in situ*. The choice of a suitable antiseptic is a matter of individual preference; many of the chlorinated bisphenols (see Antiseptics) are good germicides and are non-irritant and innocuous in ordinary concentrations. For badly burnt areas the inclusion of a local anaesthetic or analgesic is indicated, but in view of the dangers of absorption this should be chosen with care. Monash (44) studied the topical anaesthesia of unbroken skin using six different preparations in alcoholic, hydrophilic ointment base and petrolatum vehicles. A 2% alcoholic solution acted within 45–60 minutes, whilst a 5% concentration of active ingredients in the two ointments produced topical anaesthesia within 60–90 minutes. The hydrophilic ointment acted more rapidly than the petrolatum base. The effects lasted 2–4 hours. Removal of 10–15 cell layers using Scotch tape reduced the period for anaesthesia to between 1 and 4 minutes. The author suggested that the mechanism of penetration through untreated skin was entry via the follicles and lateral spreading through the follicle walls near or just below the lower level of the external barrier, and thence through the stratum mucosa to reach the papillary portions of the dermis. The treatment of a serious burn should be carried out under medical supervision.

In general greasy preparations should not be used in the treatment of sunburn. They only retain the heat of the burn and prevent the use of an antiseptic capable of mixing with the secretions and preventing bacterial infection.